



Atty. Docket WEG-2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
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Applicants: Edwin Wegman, et al.
Serial No.: 08/757,904
Filed: November 27, 1996 (as a File Wrapper
Continuation of Serial No. 08/356,112
filed December 15, 1994)
For: REDUCTION OF ADIPOSE TISSUE
Examiner: Ms. Jean C. Witz
Group Art Unit: 1651

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APPELLANTS' REPLY BRIEF

This is in reply to the Examiner's Answer of August
17, 1998.

Summary

This invention is to make people beautiful by
injecting collagenase into fat at selected sites in the
body, which results in removal of fat from those sites
where the collagenase was injected. See claims 1, 16, 20,
and dependent claims. The rejection is on §103. The
rejection is on two references, neither of which teach or

show or suggest appellants' invention. The thrust of the primary reference, Lee, et al., is to harvest microvessel cells for medicinal use. Fat is placed in vitro in a vessel and treated with a mixture including collagenase to separate out microvessel cells. Lee, et al., in passing, mentions several well-known procedures for treating patients with collagenase, but nowhere does Lee, et al., teach or show or suggest making people beautiful by injecting collagenase at selected sites of the body so that there is subsequently less fat at those sites.

The Examiner's Answer introduces and extensively argues a new issue (i.e. one not in the Final rejection), namely, a "submarine" §101 assertion of inoperability.

The Office Actions, responses, Final, and prior Brief and Examiner's Answer have focused on claim terminology. This is explored in this Reply Brief.

The important points are two-fold. First, appellants' invention is neither shown nor suggested by the prior art. Second, on the claim terminology level, it is respectfully submitted that the Office Action Final and the Examiner's Answer are in error.

Appellants' invention is an in vivo method that, for cosmetic purposes, reduces the amount of adipose tissue at

selected locations in the body by causing actual removal of adipose tissue from said locations. What happens is: (a) collagenase introduced from outside the body, causes release of fat from the tissue, and (b) biological processes within the body then metabolize residue from the adipose tissue including the released fat. Thus fat is removed from the location where the collagenase was introduced. As shown in the experimental work detailed at pages 7 through 23 of the specification, using Zucker rats, which have four well-defined subcutaneous fat pads, disruption of the adipose tissue ranged from mild to complete (Grades I to IV) depending on dosage and manner of injection. In Experiment E at page 15, lines 1-20, weight losses from the fat pads were 41%, 25% and 18%, averaging 28%; i.e., on average, over one-fourth of the substance of a fat pad had disappeared from that location.

The Examiner has hit the nail on the head in stating:

"It appears that the difference between Appellants' position in this dispute and Examiner's position is one of claim interpretation." (Page 5, lines 5-6 of Examiner's Answer.)

Because the rejection of the claims under 35 U.S.C. §103 as being unpatentable over Lee et al., combined with

Guidicelli et al., is based on the Examiner's erroneous claim interpretation, this Reply Brief will first discuss that in detail, advancing Appellants' interpretation and rebutting the Examiner's interpretation. The Reply Brief will then respond to the Examiner's assertions concerning Lee et al. and Guidicelli et al. The Examiner has not indicated that the claims would be unpatentable under 35 U.S.C. § 103 without her claim interpretation.

Claim Interpretation

Appellants' claim reducing the amount of adipose tissue at selected locations in the body by action of collagenase on the tissue.

Appellants' interpretation is that "reducing the amount" means removing adipose tissue, or causing it to disappear, from selected locations.

The Examiner's interpretation is that when collagenase acts on adipose tissue at a selected location, adipose tissue no longer exists there; hence, the amount of adipose tissue has been reduced at that location and that this much is obvious over the references (Examiner's Answer, page 7, lines 12-19).

The Examiner asserts that Appellants' analysis of the claim language is too narrow. By the same token, the

Examiner's analysis of the claim language is too narrow.
It is time to apply common sense to resolve this matter.

Appellants' interpretation, that "reducing the amount" means removing or causing to disappear, necessarily follows from the specification:

-- "Liposuction...mechanically removes fat from the subcutaneous tissues" (page 1, lines 1-4).

-- "The invention provides a new method to obtain the reduction of...excess amounts of unesthetic and/or redundant subcutaneous adipose tissue."..."In a single treatment, reduction of the tissue from its original volume may range from 25% to 75% and higher"... "The method is used to rid the patient of unwanted subcutaneous fat cells without necessity of incisions..." (page 2, lines 10-13, 17-19, 23-24).

-- "Usually for cosmetic reasons, it may be desirable to reduce the amount of subcutaneous fat at selected locations" (page 3, lines 18-20).

-- Page 15, entire:

EXPERIMENT E

No. of rats: One Zucker

Test solution: 1,000 ABC u in 0.5 mL saline

Method: 0.5 mL containing 1,000 u was injected
percutaneous in 0.1 mL amounts into three

fat pads. A fourth pad was injected with control saline.

Results: The fat pads were dissected out and weighed.

Control site upper LF -- 12.1 gm.

Test site upper RT -- 7.1 gm.

Test site lower RT -- 9.1 gm.

Test site lower LF -- 9.9 gm.

Summary/observation: At this dosage, the fat pads lost, respectively, 41%, 25% and 18% of the weight of the control pad; average loss was 28%. Based on a one sider "T" test there was a significant statistical difference between the control and test sites.

The Appellants' interpretation of the claims is supported by the specification, particularly the portions above cited, and especially Experiment E that demonstrates an average weight loss of the fat pads of over 25%, cf. claims 19 and 21.

Furthermore, the meaning of "reducing" and "reduced" is apparent from the modifying phrase:

"and the body metabolizing fat released from said adipose tissue whereby the amount of adipose tissue at

said selected locations is reduced for cosmetic purposes." Likewise, "for cosmetic purposes" modifies "reducing...the amount of adipose tissue at selected locations." Where fat is metabolized, it disappears. For cosmetic purposes to be accomplished, adipose tissue must be removed.

The Examiner, in interpreting "reducing the amount," not only relies on a narrow meaning that is at odds with the meaning dictated by the specification, but also ignores and/or minimizes the portion of the claims discussed in the preceding paragraph. The Examiner actually denies that Appellants' experimental data shows "that the bodies of the rats treated with the collagenase metabolized any of fat released" (original emphasis) (Examiner's Answer, page 9, lines 1-3); "Appellants' assertions that the fat has been metabolized is simply not supported by any evidence of record" (Examiner's Answer, page 9, last two lines).

This denial of the operability, and thus usefulness, of the invention amounts to a "submarine" rejection under 35 U.S.C. 101. It does not meet the current U.S. Patent Office guidelines on utility. Further, it is not to be found in the Final rejection. Thus, it requires no response from Appellants. However, because a rather high

proportion of the Examiner's Answer is devoted to this assertion, it is suspected that this may be the true basis of the Examiner's position; a position which is in error, and which will now be answered.

As will now be shown, the faulty reasoning on page 9 of the Examiner's Answer does not rebut Appellants' credible assertion that fat is metabolized and the logical conclusion drawn from the experimental data. Following are quotations from specified lines of page 9, and Appellants' reply thereto.

"First, it is never shown in the experimental data as to how much fat (not tissue) is released as a result of the claimed method or that the bodies of the rats treated with the collagenase metabolized any of fat released" [original emphasis] (page 9, lines 1-3).

In defining adipose tissue at page 6, lines 8-13, the Examiner had stated, inter alia, "The storage cells are called adipocytes and are the main component of the tissue mass.... Very little matrix is present in adipose tissue..." Appellants' chose Zucker rats for testing because of their well-known possession of four distinct fat pads. Since the main component of the tissue mass was adipocytes, loss of 41%, 25% and 18% of the weight of the treated fat pads in Experiment E must have involved the

disappearance of a large amount of fat. The Examiner does not deny that fat disappeared, but, wants to know where it went. Appellants say that fat is metabolized. It is removed by the body. Cf. claim 20: "...the body removing from said selected locations fat released from said adipose tissue"

"Any practitioner in the art would be aware that in the disruption of any tissue, either enzymatically or physically, some of the cells located therein will be damaged and/or destroyed. This would have been particularly expected with adipose tissue because, as stated above, the adipocytes are actually nothing more than cellular storage bags of oil" (page 9, lines 3-7).

If this is intended to suggest that, instead of being metabolized, the 28% of the substance of the fat pads in Example E constituted damaged and/or destroyed cells and that they all went somewhere else in the body, there is no support for such an idea. That adipocytes are actually nothing more than cellular storage bags of oil does not mean that they are fragile. In both Lee et al. and Guidicelli et al., adipocytes survived shaking and centrifuging.

"Further, any practitioner in the art is aware of the basic facts regarding the body's metabolism.... It is only during a reduced caloric intake...that fat is released from adipose tissue and metabolized for energy" (page 9, lines 7-11).

This acknowledges that metabolism of fat in the body occurs under some conditions, and does not deny that it could occur under other conditions.

In the remainder of page 9, i.e. lines 11-21, the Examiner is fixated on the body weight of the rats and of humans. The proposition that a weight reducing diet establishes that the metabolism of fat takes place over a period of weeks and not in two to four days, even if true, is immaterial because the gross body weight of the dieter or of the rats is not the issue. It is the weight of the fat pads of the rat that counts. The Examiner says: "As fat has mass and therefore weight, and as the weight of the rats never changed..." But the weight of the fat pads (the "selected locations") changed markedly. The weight of the whole body might change not at all, or become greater or less for a variety of reasons not related to the claimed action.

Finally, in the sentence bridging pages 9 and 10, it is contended that (a) "there is no limitation as to the

amount of fat which must be metabolized..., " and (b) "therefore, if even a small amount of that released from the adipose tissue is metabolized, such has met the claim limitations." If metabolizing a small amount meets the claim limitations, what is the problem? In any event, the claims require that an amount of collagenase be used effective for cosmetic purposes.

Concerning the first complete paragraph of page 10 of the Examiner's Answer, Appellants are not arguing the definition of "tissues." They are arguing the definition of "reducing." Examiner states that "Appellants are reading limitations into the claims that are not in fact present." But the Examiner is reading limitations into "reducing" that are contrary to the specification, and is contrived to avoid the necessity of considering the latter half of the claims reciting how fat is removed, i.e. metabolizing, as discussed in detail supra.

It is true, as stated in the paragraph bridging pages 10 and 11 of the Examiner's Answer, that Appellants represent their invention as an alternative to liposuction. On pages 1-3 of the specification, they describe certain drawbacks to liposuction and how their invention surmounts them. They also presented during prosecution articles from the medical literature reporting

trauma and deaths from liposuction. But Appellants have never claimed that one is better than the other. In medicine there are always trade-offs. It is enough that Appellants provide an unobvious alternative. Nor have Appellants argued unexpected result by comparison to liposuction. The invention is unobvious over Lee et al. and Guidicelli et al. for reasons fully set forth in their main Brief and in this Reply Brief.

The last sentence in this paragraph reveals the Examiner's insistence that Appellants' method be just like liposuction:

"There is absolutely no support in the evidence of record that the treated fat pads represent the volume of adipose tissue conventionally removed by liposuction and further, there is absolutely no evidence that the body would or even could metabolize 2.5 liters of fat released as a result of the collagenase treatment."

Simple arithmetic answers the first point. Assume that a moderately obese patient desiring liposuction would weigh 200 pounds. One liter of fat will weigh about 1.8 pounds.

$$1 \text{ liter fat} = \frac{1.8}{200} = 0.009 = 0.9\% \text{ of body weight}$$

$$2.5 \text{ liters fat} = \underline{2.5 \times 1.8} = \underline{4.5} = \underline{2.25\% \text{ of body weight}}$$

Percentage of volume loss will equal percentage of weight loss. Assume that the Zucker rat in Experiment E (page 15 of specification) weighed 350 g (the average weight of six Zucker rats in Experiment H [page 19 of specification]). The control pad in Experiment E weighed 12.1 g.

$$12.1 \text{ g} \times 28\% \text{ average loss of weight} \times 3 \text{ pads} = \frac{10,164 \text{ g}}{\text{loss}}$$

$$\frac{10,164}{350} = 0.02904 = \underline{2.9\% \text{ of body weight}}$$

As to the second point:

(a) Appellants state that "Residue from the adipose tissue in the treated location is at least partly metabolized" (specification, sentence bridging pages 6-7);

(b) 28% of the substance of the fat pads was removed from the treated locations.

Rejection on Lee et al. combined with Guidicelli et al.

To clarify the record, the claims are 1 to 21, inclusive, and all were rejected under 35 U.S.C. § 103 as being unpatentable over Lee et al. combined with Guidicelli et al. Independent claims 1 and 20 call for the introduction of collagenase or collagenase plus another proteinase. Independent claim 16 only specifies collagenase but does not exclude another proteinase. All

claims are drawn to a method of reducing adipose tissue for cosmetic purposes. Claim 19 and 21 specify numerical percentages of reduction of adipose tissue.

Lee et al. use compositions of collagenase plus chymopapain to digest connective tissues. Their principal interest is in isolating, in vitro, viable microvessel cells embedded in such tissues. They prefer to use liposuctioned adipose tissue as the raw material from which they isolate microvessel cells. Released microvessel cells, and also released adipocytes (fat cells) survive the digestion. Lee et al. also state that their compositions can be used in vivo for the treatment of seven specific maladies (column 7, line 67, through column 8, line 7), all of which are very specific.

Guidicelli et al. prepared fat cells by in vitro digestion of adipose tissue with collagenase plus trypsin. As in Lee et al., the fat cells (adipocytes) survived the digestion.

The Examiner asserts that it would be obvious to choose to digest any one of the numerous connective tissues found throughout the body. Lee et al. name seven specific pathologies, each with its own specific location in the body. There is no indication at all of what happens subsequent to digestion of any of those particular

connective tissues. The Examiner then asserts that Appellants' claims call only for the reduction of adipose tissue. Elsewhere, "This is all that is required of the claimed method" (page 6, lines 5-6), and "no adipose tissue exists" (page 7, lines 18-19). But Appellants' claims do recite that: "the body metabolizing fat released from said adipose tissue whereby the amount of adipose tissue at said selected locations is reduced for cosmetic purposes" (claim 1); "the body removing from said selected locations fat released from said adipose tissue whereby the amount of adipose tissue at said locations is reduced for cosmetic purposes" (claim 20). Such removing of a component of a digested connective tissue in the body is not suggested by nor derivable from Lee et al., who deals with liposuctioned tissue only in vitro, where released fat cannot be metabolized and, in fact, released adipocytes survive the digestion (column 8, lines 45-51; column 11, lines 22-27).

In the Examiner's Answer at page 4, lines 15-20, continuing at page 5, line 1, "for cosmetic purpose" in Appellants' claims is dismissed as not patentably distinguishing the claims over the disclosure of Lee et al. It has been pointed out in the first section of this Reply Brief that these words modify and hence clarify the

meaning of "reduced." Further, if the particular fatty cysts referred to by the Examiner present a cosmetic problem, the claims are satisfied.

Turning now to the paragraph bridging pages 6 and 7 of the Examiner's Answer, it is stated that Appellants "suggest that col. 8, lines 45-51 [of Lee et al.] provides evidence that all the adipocytes survive intact" (emphasis added). Appellants did not say "all." Lee et al. teach that upon centrifuging, "adipocytes and a supernatant are separated from the microvessel cells." That no evaluation of the supernatant is disclosed is irrelevant. The Examiner says, "it is expected that in both cases [Appellants and Lee et al.] the resulting hydrolysis of the matrix that at least some of the fat cells will be damaged and disrupted, thereby releasing the oil within." This is impermissibly using Appellants' own teaching to interpret what might have happened in the prior art, on which the prior art is silent.

Lee et al. were seeking to isolate and preserve microvessel cells, and during that procedure adipocytes were also recovered; Guidicelli et al. were seeking to and did isolate adipocytes. Appellants point to these in vitro objectives and results to contrast with their in

vivo procedure in which the objective, successfully achieved, is to get rid of adipocytes.

In the middle of the large paragraph of page 7, the Examiner says (for the first time) that "Appellants' use of the phrase "the connective tissue of adipose tissue" is not clear. It is submitted that one skilled in the art will have no trouble understanding this. Later in the same paragraph, the Examiner explains how "As a result of disaggregation of these cells by dissolution of the connective tissue matrix, the tissue has been digested." See Lee et al., column 7, line 17, "connective tissue, which holds cells together."

Page 8, lines 7-8 of the Examiner's Statement states "there is no [claim] limitation as to the disappearance of fat from the selected locations." Not ipso verbum, but when fat is metabolized, it is no longer there. The Examiner, who insists that "tissue is no longer there," can't have it both ways.

At page 8, lines 10-13: "there is no limit on the amount or volume of adipose tissue to be treated. [True.] Therefore, claims to the percentage [i.e., claims 19 and 21] of adipose tissue reduced as a result of the treatment are dependent upon the amount of tissue treated in the first place." This reveals a lack of understanding of the

meaning of percentage. It has nothing to do with the amount of tissue treated. If the Examiner enters a store where all prices are reduced by 25%, she will save \$10 on a \$40 item, save \$25 on a \$100 item, etc. Regardless of the original price and the amounts saved, the percentage saved is always the same.

The same error appears at page 11, lines 5-8 of the Examiner's Answer, referring to the GROUPING OF CLAIMS in Appellants' Brief at page 3, lines 11-15, and page 11, line 21 continuing on page 12, lines 1-3.

* * *

The Examiner has not indicated, either in the Final Rejection or in the Examiner's Answer, that Appellants' claims would be unpatentable under 35 U.S.C. § 103 without her claim interpretation.

That interpretation either

- deletes the last half of the claims as irrelevant (i.e., the amount of tissue is already reduced at the site because it no longer exists as a tissue)

or

- asserts that the last half of the claims lack utility (i.e., the method doesn't mimic liposuction because fat is not removed from the body, and/or the body would not or could not metabolize fat.

It is axiomatic that claims are to be read in light of the specification. The Examiner has not done this. When the claims are so read, they properly describe Appellants' patentable invention.

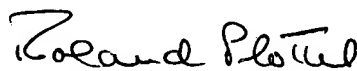
Conclusion

The rejection is on §103. The rejection, however, ignored the last half of Appellants' claims 1, 16 and 20 (on which all the other claims depend). The Final rejection is based as if half of the claims' text were missing. Much of the Examiner's Answer is devoted to assertion that the description in the last half of these claims does not work. But, the last half of these claims is supported by Appellants' specification. Further, the assertion of non-utility is not in the Office Action Final.

An important point is that Lee, et al., do not teach anything about in vivo fat reduction, which is the object and teaching of Appellants' invention and claims.

The prior art does not show, and does not suggest, Appellants' invention.

Respectfully submitted,



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